

***Remarks***

By this Amendment, claims 64, 70-71, 79, 89, 91, 95, 100, 104, 108-110, 112, 115 and 119-122 are sought to be amended and new claims 123-135 are sought to be entered. Additionally, claims 69 and 90 are cancelled without prejudice to or disclaimer of the subject matter encompassed by these claims. Support for the amendments to the claims can be found throughout the specification as filed. Specifically, support for claims 123-124, 126-129, 131-132 and 134-135 can be found at page 16, lines 4-28 of the specification. Support for claims 125, 130 and 133 can be found at page 17, lines 7-20 and at page 21, lines 1-14 of the specification. No new matter has been introduced. Upon entry of these amendments, claims 64-68, 70-89 and 91-135 are pending, with claims 64, 79, 89, 104 and 119 being the independent claims.

***I. Summary of the Office Action***

In the Office Action dated October 6, 2003, the Examiner made one rejection of the claims. Based on the following remarks, Applicants respectfully request that the Examiner reconsider the outstanding rejection and that it be withdrawn. Objection to the Specification

***II. The Rejection of Claims 64-122 Under 35 U.S.C. § 102(e) as Anticipated by or, in the Alternative, Under 35 U.S.C. § 103(a) as Obvious Over Spinella et al. Must be Withdrawn***

In the Office Action at pages 2 through 5, claims 64-122 were rejected under 35 U.S.C. § 102(e) as being anticipated by, or in the alternative, under 35 U.S.C. § 103(a) as obvious over Spinella *et al.* (United States patent no. 5,968,784; hereinafter "Spinella"). Applicants respectfully traverse this rejection, and request its

reconsideration and withdrawal.

**A. Rejection Under 35 U.S.C. § 102(e)**

Claims 69 and 90 have been cancelled without prejudice or disclaimer, thus rendering this rejection moot with respect to these claims.

Claims 64, 79, 89, 104 and 119 are the independent claims. Claims 64, 79, 89, 104 and 119 are drawn to a method of making one or more cDNA molecules, wherein, *inter alia*, the one or more cDNA molecules are cleaved with not more than one enzyme at a cleavage site within the primer-adaptor. Claims 65-68, 70-78 and 123-125 depend, directly or indirectly, from claim 64. Claims 80-88 and 126-127 depend directly from claim 79. Claims 91-103 and 128-130 depend, directly or indirectly, from claim 89. Claims 105-118 and 131-133 depend, directly or indirectly, from claim 104. Claims 120-122 and 134-135 depend directly from claim 119.

A claimed invention is anticipated under 35 U.S.C. § 102 only if there is "[d]isclosure in a single piece of prior art of each and every limitation of a claimed invention." *Apple Computer, Inc. v. Articulate Systems, Inc.*, 234 F.3d 14, 20, 57 USPQ2d 1057, 1061 (Fed. Cir. 2000)). As noted above, all of the currently pending claim claims are drawn to methods in which cDNA molecules are cleaved, within the primer-adaptor, with not more than one enzyme. In contrast, Spinella does not disclose methods in which cDNA molecules are cleaved with not more than one enzyme at a cleavage site within the primer-adaptor. Instead, the methods of Spinella involve cleavage using at least *two* enzymes. *See, e.g.*, Spinella, column 7, lines 13-14. Hence, Spinella cannot and does not anticipate any of the currently pending claims.

In support of this rejection, the Examiner asserted that "[t]he method of Spinella *et al.* involves preparing double-stranded cDNA from an mRNA using a primer, cleaving the double stranded cDNA with a first restriction site [sic, enzyme] and inserting the cDNA inserts into cloning vector (See column 5, lines 40-55) . . . ." Office Action, page 3. Applicants wish to point out, however, that the portion of Spinella referred to by the Examiner does not disclose cleaving the cDNA molecules with not more than one enzyme at a cleavage site within the primer-adaptor as recited in the present claims.

The method of Spinella is set forth schematically in Figure 2 of that reference. As can be seen in the figure, after preparing a cDNA molecule, the cDNA molecule is digested with *two* restriction enzymes in order to generate a fragment of the cDNA molecule. Moreover, in the portion of Spinella relied upon by the Examiner, this reference clearly discloses that the cDNA molecule is *not* cleaved within the primer-adaptor: "cleaving said double-stranded cDNAs with a first restriction endonuclease *which cleaves at a site within said cDNA sequence and not within said primer . . .* ." Spinella, column 5, lines 42-44 (emphasis added); *see also* Spinella, column 6, lines 24-26, and column 14, lines 28-30. Figure 2 of Spinella clearly shows the generation of fragments of double-stranded cDNA prior to ligating the fragments into a vector using *two* restriction enzymes (*Mbo*I and *Not*I). In addition, in Example 2, Spinella discloses preparing double-stranded cDNA, and states that "[t]he cDNA sample is then cleaved with *Mbo*I and *Not*I. The cDNA vector sample is then inserted into the TALEST vector depicted in FIG. 2." Spinella, column 17, lines 8-10. Thus, Spinella discloses only inserting or ligating a cDNA molecule into a vector, wherein the cDNA molecule is cleaved by *two* restriction enzymes. Accordingly, Spinella does not anticipate the invention as presently claimed.

For at least the foregoing reasons, Applicants respectfully submit that Spinella does not disclose the invention as presently claimed. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(e).

**B. Rejection Under 35 U.S.C. § 103(a)**

The Examiner has also alternatively rejected claims 64-122 under 35 U.S.C. § 103(a) over Spinella. Applicants respectfully traverse this rejection.

In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. *See In re Piasecki*, 223 USPQ 785, 787-88 (Fed. Cir. 1984). In pertinent part, the MPEP states that "[t]o establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." MPEP 2143.03, *citing In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). In addition, "there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings." MPEP 2143. Further, "[i]f proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion to make the proposed modification." MPEP 2143.01 *citing In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). Under these standards, Spinella cannot be used to support a *prima facie* case of obviousness.

As discussed above, Spinella does not disclose all of the elements of the present claims. Further, there is no motivation that would have led one skilled in the art to modify the method disclosed by Spinella to reach the methods presently claimed, because such modification would render Spinella unfit for its intended purpose.

The purpose of Spinella is to generate RNA sequence tags that can be used to evaluate gene expression in cells. *See* Spinella, column 13, lines 57 to column 14, line 7. The tags are prepared by directionally cloning a fragment of the cDNA into a specially designed vector such that the 5'-end of every cDNA fragment begins with the restriction site used to cleave within the cDNA molecule. *See* Spinella, column 14, lines 44-48, and Figure 2. The vector contains two Type II restriction enzyme recognition sequences arranged next to the site into which the 5'-end of the fragment is cloned. *See* Spinella, column 14, line 50 to column 15, line 22. Digestion with the two Type II restriction enzymes produces a tag containing a small portion of the sequence of the original cDNA. *See* Spinella, column 15, lines 14-22. In order to produce the tags, the cDNA molecule must be cleaved into a fragment having the required 5'-end so that it can be cloned into the vector in the proper relationship to the Type II restriction enzyme recognition sequences. Hence, to be suitable for their intended purpose, the methods disclosed in Spinella *require* digestion of the cDNA molecules with at least *two* restriction enzymes. Modification of Spinella such that the cDNA molecules are cleaved with not more than one enzyme, as recited in the present claims, would make it impossible to produce the RNA tags, thereby rendering the method of Spinella unfit for its intended purpose. Accordingly, one of ordinary skill would *not* have been motivated to modify the disclosure of Spinella to cleave the cDNA molecules with not more than one enzyme. Indeed, Spinella teaches *away* from making such a modification, since modifying the methods of Spinella in this way would render the methods of that reference useless for their intended purpose. Accordingly, Spinella cannot render obvious the presently claimed invention.

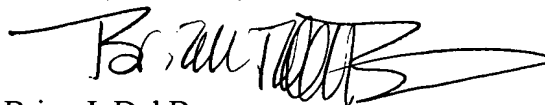
Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness of the presently claimed invention. Reconsideration and withdrawal of this rejection are therefore respectfully requested.

***Conclusion***

Applicants believe that a full and complete reply to the Office Action has been made, and that the present application is in condition for allowance. Prompt entry and favorable consideration of this reply is respectfully requested. Should the Examiner believe, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

A handwritten signature in black ink, appearing to read "Brian J. Del Buono", with a long horizontal flourish extending to the right.

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